MAY -2 2008 K081030

Prodesse

Real Time Solutions

510(k) SUMMARY

April 8, 2008

CONTACT

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NAME OF DEVICE

Trade Name:	ProFlu+ Assay
Regulation Number:	21 CFR 866.3980
Classification Name:	Respiratory Viral Panel Multiplex Nucleic Acid Assay

PREDICATE DEVICE

K073029 – ProFlu+ Assay, Prodesse, Inc.
K063765 – ID-Tag Respiratory Virus Panel, Luminex Molecular Diagnostics, Inc.

INTENDED USE

The ProFlu+™ Assay is a multiplex Real Time RT-PCR *in vitro* diagnostic test for the rapid and qualitative detection and discrimination of Influenza A Virus, Influenza B Virus, and Respiratory Syncytial Virus (RSV) nucleic acids isolated and purified from nasopharyngeal (NP) swab specimens obtained from symptomatic patients. This test is intended for use to aid in the differential diagnosis of Influenza A, Influenza B and RSV viral infections in humans and is not intended to detect Influenza C.

Negative results do not preclude influenza or RSV virus infection and should not be used as the sole basis for treatment or other management decisions. It is recommended that negative RSV results be confirmed by culture.

Performance characteristics for Influenza A Virus were established when Influenza A/H3 and A/H1 were the predominant Influenza A viruses in circulation. When other Influenza A viruses are emerging, performance characteristics may vary.

If infections with a novel Influenza A virus is suspected based on current clinical and epidemiological screening criteria recommended by public health authorities, specimens should be collected with appropriate infection control precautions for novel virulent Influenza viruses and sent to state or local health department for

PRODUCT DESCRIPTION

The ProFlu+ Assay enables detection and differentiation of Influenza A Virus, Influenza B Virus, Respiratory Syncytial Virus (RSV) (Types A and B), and Internal Control. Nasopharyngeal swab specimens are collected from symptomatic patients using a polyester, rayon or nylon tipped swab and place into viral transport medium.

An Internal Control (IC) is added to each sample prior to nucleic acid isolation to monitor for inhibitors present in the specimens. The isolation and purification of the nucleic acids is performed using either a MagNA Pure LC Instrument (Roche) and the MagNA Pure Total Nucleic Acid Isolation Kit (Roche) or a NucliSENS® easyMAG™ System (bioMérieux) and the Automated Magnetic Extraction Reagents (bioMérieux).

The purified nucleic acids are added to ProFlu+ Supermix along with enzymes included in the ProFlu+ Detection Kit. The ProFlu+ Supermix contains oligonucleotide primers and target-specific oligonucleotide probes. The primers are complementary to highly conserved regions of genetic sequences for these respiratory viruses. The probes are dual-labeled with a reporter dye attached to the 5'-end and a quencher dye attached to the 3'-end.

Reverse transcription of the RNA in the sample into complementary DNA (cDNA) and subsequent amplification of DNA is performed in a Cepheid SmartCycler® II instrument. In this process, the probe anneals specifically to the template followed by primer extension and amplification. The ProFlu+ Assay is based on Taqman chemistry, which utilizes the 5' – 3' exonuclease activity of the Taq polymerase to cleave the probe thus separating the reporter dye from the quencher. This generates an increase in fluorescent signal upon excitation from a light source. With each cycle, additional reporter dye molecules are cleaved from their respective probes, further increasing fluorescent signal. The amount of fluorescence at any given cycle is dependent on the amount of amplification products present at that time. Fluorescent intensity is monitored during each PCR cycle by the SmartCycler instrument.

SUBSTANTIAL EQUIVALENCE

Clinical Performance

Performance characteristics of the ProFlu+ Assay were established during a prospective study at 3 U.S. clinical laboratories and a retrospective study at 1 U.S. site during the 2006-2007 respiratory virus season (February – April). Samples used for this study were nasopharyngeal (NP) swab specimens that were collected for routine influenza or RSV testing by each site.

The reference method was rapid culture (shell vial) followed by direct fluorescent antibody (DFA) screening and identification.

A total of 891 NP swab samples were tested with the ProFlu+ Assay and by culture. Five (5) samples that initially gave unresolved results remained unresolved upon retesting with the ProFlu+ Assay and are not included in the analysis below. All 5 samples were culture negative.

A total of 23 samples were DFA Respiratory Virus Screen positive (screening reagent detects Influenza A and B, RSV, Parainfluenza 1, 2 and 3 and Adenovirus), but contained too few cells to obtain a specific positive identification. 21 of these 23 samples were also positive by the ProFlu+ Assay (9 Influenza A, 11 Influenza B and 1 RSV positives) and genetic sequencing analysis confirmed the identification of the specific virus. The other 2 DFA screen positive samples were negative by the ProFlu+ Assay and sequence analysis confirmed that they were negative for Influenza A, Influenza B and RSV; these 2 samples were considered true negatives. Discrepant analysis for samples where ProFlu+ Assay and culture results were in disagreement was performed using RT-PCR with virus specific primers obtained from literature followed by sequencing.

Results from Prospective Study:

Influenza A Comparison Results

		Reference Method			
		Positive	**Negative**	**Total**	**Comments**
ProFlu+ Assay	**Positive**	127	52 [a]	**179**	Sensitivity 100% (97.1% - 100%) 95% CI
	Negative	0	647	**647**	Specificity 92.6% (90.4% - 94.3%) 95% CI
	Total	**127**	**699**	**826**	

[a] *Forty-three (43) samples positive for Influenza A by sequence analysis, 8 samples negative for Influenza A by sequence analysis, and 1 sample unavailable for sequence analysis.*

Influenza B Comparison Results

		Reference Method			
		Positive	**Negative**	**Total**	**Comments**
ProFlu+ Assay	**Positive**	45	11 [a]	**56**	Sensitivity 97.8% (88.7% - 99.6%) 95% CI
	Negative	1 [b]	769	**770**	Specificity 98.6% (97.5% - 99.2%) 95% CI
	Total	**46**	**780**	**826**	

[a] *Eleven (11) samples positive for Influenza B by sequence analysis.*
[b] *One (1) sample negative for Influenza B by sequence analysis.*

RSV Comparison Results

		Reference Method			
		Positive	Negative	Total	
ProFlu+ Assay	Positive	34 [a]	40 [a]	74	Sensitivity 89.5% (75.9% - 95.8%) 95% CI
	Negative	4 [b]	748	752	Specificity 94.9% (93.2% - 96.2%) 95% CI
	Total	38	788	826	

[a] *Thirty-four (34) samples positive for RSV by sequence analysis, 3 samples negative for RSV by sequence analysis, and 3 samples unavailable for sequence analysis.*
[b] *One (1) sample positive for RSV by sequence analysis and 3 samples negative for RSV by sequence analysis.*

Results from Retrospective Study

Influenza A Comparison Results

		Reference Method			
		Positive	Negative	Total	Comments
ProFlu+ Assay	Positive	5	2 [a]	7	Sensitivity 100% (56.6% - 100%) 95% CI
	Negative	0	53	53	Specificity 96.4% (87.7% - 99.0%) 95% CI
	Total	5	55	60	

[a] *One (1) samples positive for Influenza A by sequence analysis and 1 sample negative for Influenza A by sequence analysis*

Influenza B Comparison Results

		Reference Method			
		Positive	Negative	Total	Comments
ProFlu+ Assay	Positive	17	0	17	Sensitivity 89.5% (68.6% - 97.1%) 95% CI
	Negative	2 [a]	41	43	Specificity 100% (91.4% - 100%) 95% CI
	Total	19	41	60	

[a] *Two (2) samples positive for Influenza B by sequence analysis.*

RSV Comparison Results

		Reference Method			
		Positive	Negative	Total	
ProFlu+ Assay	Positive	23	1 [a]	24	Sensitivity 100% (85.7% - 100%) 95% CI
	Negative	0	36	36	Specificity 97.3% (86.2% - 99.5%) 95% CI
	Total	23	37	60	

[a] *One sample positive for RSV by sequence analysis.*

Reproducibility

The reproducibility of the ProFlu+ Assay was evaluated at 3 laboratory sites. Reproducibility was assessed using a panel of 10 simulated samples that included medium and low (near the assay limit of detection) Influenza A, Influenza B, or RSV positive and negative samples. Panels and controls were tested at each site by 2 operators for 5 days (10 samples and 5 controls X 2 operators X 5 days X 3 sites = 450). The overall percent agreement for the ProFlu+ Assay was 98%.

Panel Member ID	Site 1			Site 2			Site 3			Total Agreement with expected result (%)	95% Confidence Interval
	Agreement with expected result	AVE C_T	%CV	Agreement with expected result	AVE C_T	%CV	Agreement with expected result	AVE C_T	%CV		
Negative (2 Panel Members)	20/20	30.5	3.2%	20/20	31.2	7.1%	19*/20	32.2	2.4%	59/60 (98%)	91% - 100%
Influenza A Low Positive	10/10	36.0	3.3%	9/10	36.4	3.9%	7/10	37.8	5.3%	26/30 (87%)	70% - 95%
Influenza A Medium Positive	10/10	32.6	1.4%	10/10	33.4	4.0%	10/10	33	2.5%	30/30 (100%)	89% - 100%
Influenza B Low Positive	10/10	32.7	1.4%	10/10	32.6	1.4%	10/10	32.2	1.9%	30/30 (100%)	89% - 100%
Influenza B Medium Positive	10/10	30.5	1.3%	10/10	30.1	0.7%	10/10	29.7	0.8%	30/30 (100%)	89% - 100%
RSV A Low positive	8/10	30.1	8.3%	8/10	32.5	6.2%	8/10	30.7	6.8%	24/30 (80%)	63% - 90%
RSV A medium positive	10/10	29.5	3.0%	10/10	29.5	3.0%	10/10	29.2	2.7%	30/30 (100%)	89% - 100%
RSV B low positive	10/10	31.9	3.5%	10/10	32.3	5.5%	10/10	31.8	5.1%	30/30 (100%)	89% - 100%
RSV B medium positive	10/10	29.5	1.9%	10/10	29.5	4.0%	10/10	28.7	4.2%	30/30 (100%)	89% - 100%
Influenza A RNA Control	10/10	33.5	1.6%	10/10	32.9	4.2%	10/10	34.4	0.9%	30/30 (100%)	89% - 100%
Influenza B RNA Control	10/10	32.8	1.4%	10/10	32.1	3.1%	10/10	33.8	1.3%	30/30 (100%)	89% - 100%
RSV A RNA Control	10/10	33.7	1.8%	10/10	32.3	3.1%	10/10	34.8	1.5%	30/30 (100%)	89% - 100%
RSV B RNA Control	10/10	32.1	1.6%	10/10	31.9	4.3%	10/10	35.2	2.5%	30/30 (100%)	89% - 100%
Negative Control	10/10	28.9	4.0%	10/10	29.6	5.2%	10/10	30.2	1.4%	30/30 (100%)	89% - 100%
Total Agreement All	**148/150 (99%)**			**147/150 (98%)**			**144/150 (96%)**			**439/450 (98%)**	**96% - 99%**

*1 negative sample Unresolved (IC = FAIL). C_T values for Influenza A, Influenza B and RSV were negative, however.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

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MAY - 2 2008

Re: k081030
Trade/Device Name: ProFlu™ Plus
Regulation Number: 21 CFR 866.3980
Regulation Name: Respiratory viral panel multiplex nucleic acid assay
Regulatory Class: Class II
Product Code: OCC
Dated: April 25, 2008
Received: April 28, 2008

Dear Dr. Harrington:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820). This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at 240-276-0450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding postmarket surveillance, please contact CDRH's Office of Surveillance and Biometric's (OSB's) Division of Postmarket Surveillance at 240-276-3474. For questions regarding the reporting of device adverse events (Medical Device Reporting (MDR)), please contact the Division of Surveillance Systems at 240-276-3464. You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (240) 276-3150 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

Indication for Use

510(k) Number (if known): K081030

Device Name: ProFlu+ Assay

Indication For Use:

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Negative results do not preclude influenza or RSV virus infection and should not be used as the sole basis for treatment or other management decisions. It is recommended that negative RSV results be confirmed by culture.

Performance characteristics for Influenza A Virus were established when Influenza A/H3 and A/H1 were the predominant Influenza A viruses in circulation. When other Influenza A viruses are emerging, performance characteristics may vary.

If infections with a novel Influenza A virus is suspected based on current clinical and epidemiological screening criteria recommended by public health authorities, specimens should be collected with appropriate infection control precautions for novel virulent Influenza viruses and sent to state or local health department for testing. Viral culture should not be attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens.

Prescription Use ___X___ (21 CFR Part 801 Subpart D) And/Or Over the Counter Use ____. (21 CFR Part 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE; CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD)

Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety

510(k) K081030